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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/765,108	03/27/97	KRIEGER M	MIT6620CIP

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EXAMINER	
ULM, J	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/03/98

Please find below and/or attached an Office communication concerning this application or proceeding.

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Please find below a communication from the EXAMINER in charge of this application.

Commissioner of Patents

Please see the Advisory Action attached hereto.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm at telephone number (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Advisory Action

Application No.	Applicant(s)
08/765,108	Krieger et al.
Examiner	**Group Art Unit**
John Ulm	1646

THE PERIOD FOR RESPONSE: [check only a) or b)]

a) ☒ expires *four* months from the mailing date of the final rejection.

b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☐ Appellant's Brief is due two months from the date of the Notice of Appeal filed on _____ (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on *Jul 23, 1998* has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:

☒ The proposed amendment(s):

☒ will be entered upon filing of a Notice of Appeal and an Appeal Brief.

☐ will not be entered because:

☐ they raise new issues that would require further consideration and/or search. (See note below).

☐ they raise the issue of new matter. (See note below).

☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: _____

☒ Applicant's response has overcome the following rejection(s):
NONE

☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.

☐ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:

☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: *NONE*

Claims objected to: *NONE*

Claims rejected: *9-15, 19-22, and 44-50*

☐ The proposed drawing correction filed on _____ ☐has ☐has not been approved by the Examiner.

☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ .

☒ Other *SEE ATTACHED*

JOHN ULM
PRIMARY EXAMINER
ART UNIT 1646

Claims 9 to 15, 19 to 22 and 44 to 50 are pending in the instant applications.

The amendment filed 23 July of 1998 under 37 CFR 1.116 in reply to the final rejection will be entered upon the filing of an appeal, but is not deemed to place the application in condition for allowance.

Applicant's narrow interpretation of the recent decision in *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), as being limited to a cDNA/'protein relationship is unfounded. The court held that :

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for

isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

This court decision clearly supports the instant rejection of record.

Applicant argument that the claims are not unduly broad because the instant specification provides assays which "allow those skilled in the art to determine which variants are functional and which are not functional is legally unsound. Applicant has apparently taken the position that 35 U.S.C. § 112, first paragraph, permits an artisan to present claims of essentially limitless breadth so long as the specification provides one with the ability to test any particular embodiment which is encompassed by the material limitations of a claim and thereby distinguish between those embodiments which meet the functional limitations from those embodiments which don't. This argument is not entirely without merit. However, the issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. Applicant's 'make and test' position is inconsistent with the decisions in *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) and *Amgen v. Chugai Pharmaceuticals Co. Ltd.*, 13 USPQ2d, 1737 (1990), which were cited as the judicial basis for the instant rejection in the previous office action, and *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988). *In re Wands* stated that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the

invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of this factors were addressed in the initial rejection. The current claims encompass non-naturally occurring proteins having an amino acid sequences which deviates from the naturally occurring amino acid sequence by an unspecified number amino acid residues. Because the hybridization limitations of the claims is unconditional, it places no additional limitations on the claimed subject matter. Therefore, claim 9, for example, is a single means claim because it encompass an antibody which binds to any protein having the recited activity irrespective of the structure of that protein. A single means claim, i.e., where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph. In re Hyatt , 708 F.2d 712,>714 - 715,< 218 USPQ 195>, 197< (Fed. Cir. 1983) (A single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor.). When claims depend on a recited property, a fact situation comparable to Hyatt is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. See M.P.E.P. 2164.08(a). Breadth alone is not the issue, however. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was

made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Having established the breadth of the claims, *Wands* now requires that one consider the number of working examples presented in the instant specification. It is noted that there in not a single example in the instant specification, working or prophetic, of any protein whose amino acid sequence deviates from nature. Since there are **no** working examples, then one must consider the guidance provided by the instant specification and the prior art of record. The instant specification provides absolutely no guidance as to which amino acid residues in SEQ ID NO:4 of the instant application are essential for the functional and structural integrity of a scavenger receptor protein and which residues are either substitutable or expendable. Further, there is no functionally and structurally analogous protein which has been identified in the prior art for which this information is known and could be extrapolated to the scavenger receptor protein of the instant invention by analogy. In conclusion, the instant claim encompasses a vast, almost limitless, number of antibodies which bind to proteins having non-naturally occurring amino acid sequences and proteins having native amino acid sequence which are not disclosed in the instant specification

and yet the instant specification provides no working examples and no guidance that would permit and artisan to practice the invention commensurate with the scope of the instant claims.

Applicant's argument is based upon a premise that the standard under 35 U.S.C. ¶ 112, first paragraph, is that of mutating a subject protein and testing to see if it retains the desired biological activity is a position that has been routinely dismissed by the courts, as shown by those decisions cited above.

Further, *In re Wands* determined that the repetition of work which was disclosed in a patent application as producing a composition containing an antibody, which is a naturally occurring compound, did not constitute undue experimentation even if the antibody produced thereby was not identical to those that were disclosed in that application. The instant claims are not limited to naturally occurring compounds and the instant specification does not provide a description of a repeatable process of producing a scavenger receptor protein whose amino acid deviates from the single disclosed, naturally occurring sequence. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues in the amino acid sequence of SEQ ID NO:4 which are required for the functional and structural integrity of that protein. It is this additional characterization of that single disclosed, naturally occurring, protein that is required in order to obtain the functional and structural data needed to permit one

to produce an antibody to a scavenger receptor protein which meets both the structural and functional requirements of the instant claims that constitutes undue experimentation.

Applicant's argument that claim 49 is not limited to *in vivo* methods ignores that fact that it encompasses them. A claim must be commensurate in scope with the disclosure. This claim encompasses an *in vivo* method of treatment and yet the instant application does not provide the needed guidance. To practice such a method would require a knowledge of the route, duration and quantity of administration of that protein to a subject and this information is not provided by the instant specification. The text on pages 42 and 43 of the instant specification clearly fails to supply the guidance that would be needed by a routine practitioner. The instant specification has also failed to disclose how these parameters are to be determined, how a similar method was practiced in the art with a different agent or to provide even a single working example, prophetic or actual, of the claimed method. In the absence of this guidance a practitioner would have to resort to a substantial amount of undue experimentation involving the variation in the amount and duration of administration of a scavenger receptor protein of the instant invention and in determining a suitable route of administration. The instant situation is directly analogous to that which was addressed in *In re Colianni*, 195 U.S.P.Q. 150,(CCPA 1977), which held that a "[d]isclosure that calls for application of "sufficient" ultrasonic energy to practice claimed method of fusing bones but does not disclose what "sufficient" dosage of ultrasonic energy might be or how those skilled in the art might select appropriate intensity, frequency, and duration, and

contains no specific examples or embodiment by way of illustration of how claimed method is to be practiced does not meet requirements of 35 U.S.C. 112 first paragraph".

Applicant's assertion that claims 44 to 50 are not incomplete because "the claimed methods in conjunction with the specification are absolutely clear and complete". Applicant's own statement concedes to the rejection since one can not rely upon the specification to complete the claims, only to interpret the meaning of the terms recited there. To be complete, a claim must recite sufficient elements to complete the invention. One can not properly rely upon the specification to provide those elements which are lacking from the claims. This is also true for functional limitations such as hybridizing".

Applicant's arguments filed 23 July of 1998 have been fully considered but they are not persuasive.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached at (703) 308-2957.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN ULM
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